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editorial

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The innovative medicines initiative: a pre-competitive initiative to enhance the biomedical science base of Europe to expedite the development of new medicines for patients

Significant challenges face biomedical research and development in Europe and the rest of the world. The costs of bringing a new medicine to market are now estimated to be over £1 billion [1,2] and attrition rates have, if anything, increased over those of the late 1990s. This is due to the high percentage of completely novel therapeutic approaches reaching clinical trials. In addition, demographic changes, which are present not only in Europe but also in the rest of the developed and the developing world, have led to an increase in the prevalence of chronic diseases and diseases of old age (WHO priority report: http://mednet3.who.int/prioritymeds/report/final18october.pdf). The development of new medicines for these disorders has been historically challenging. This, coupled with the increased risk of working on innovative targets has driven a re-evaluation of the traditional model of research and development. There is a realisation by public and private stakeholders that this model is not sustainable in the long term, and companies are seeking new ways to decrease attrition, especially in later phase development. Such public–private partnerships have been established in other areas of research, such as genomics. For example, in April 1999, ten large pharmaceutical companies and the U.K. Wellcome Trust philanthropy announced the establishment of a consortium to find and map 300 000 common single nucleotide polymorphisms (SNPs).

Over the past two decades, the pharmaceutical industry made significant improvements in areas such as pharmacokinetics, such that the major reasons now for failure in early drug development are efficacy and unpredictable toxicity. The advances in genomics and other technologies, such as non-invasive imaging, provide a real opportunity to develop methodologies to improve predictions with regard to both efficacy and toxicity. Already genomic techniques have provided better target validation in drug discovery, as has already been demonstrated in the field of oncology. However, the real power of much of this technology lies in its potential to generate predictive biomarkers. For example, such biomarkers could be used to predict whether a particular compound is likely to cause cardiomyopathy after long-term administration, or to increase the relative risk of developing a particular carcinoma. Not only would this reduce late-phase attrition, but it would also considerably reduce cycle times in early development. Ultimately this type of research has the potential to reduce the numbers of animals used in the drug

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discovery and development process. In addition, increased investment for, and advances in, proteomics, transcriptomics, metabolomics and systems biology will also provide a framework for the discovery and validation of surrogate and pharmacodynamic end-points. To make real progress in harnessing these advances in a reasonable time frame would require an investment far greater than any one company or traditional public/private consortia could bear.

This has led to the rise of public–private initiatives such as the Critical Path initiative in the USA—this is the FDA's initiative to stimulate a national effort to modernise the scientific process through which a potential human drug, biological product or medical device is transformed from a discovery of proof of concept into a medical product. Globally there is recognition of the need for more exchange of information and dialogue between all key stakeholders (academia, industry, physicians, regulators and patient groups) with an interest in expediting new medicines development. In 2004, the Research Directors Group of the European Federation of Pharmaceutical Industries (EFPIA) was asked by the EU Commission to identify key bottlenecks in the process of new medicines discovery and development that could benefit from shared resources and expertise across industry and academia. These bottlenecks were subsequently endorsed at a meeting of key stakeholders in October 2004. It was proposed at the time that the best vehicle for taking this forward was via a new funding mechanism that had arisen from the Seventh Framework programme, the Joint Technology Initiative (JTI).

This would be such a large undertaking; separate funds were sought under Framework VI to develop a Strategic Research Agenda (SRA) that would form the blue print for the JTI proposal. To test the model, as part of the same funding proposal, a pilot project, Innomed, was included. This was to begin the pre-competitive dialogue in a few selected areas (Alzheimer's disease and predictive toxicology) and to identify some of the opportunities and pitfalls that such pre-competitive research could provide. Innomed was approved under Framework VI and over the next 18 months, the details of the larger JTI proposal (The Innovative Medicines Initiative (IMI)) were fleshed out and brought together to form a research outline that was presented to the European Commission (The IMI Strategic Research Agenda at http://www.imi-europe.org). Real progress was made during 2007 with the adoption of the legal package by the Commission, Competitiveness Council and the European Parliament. In December 2007, the European Council finally approved the establishment of the IMI Joint Undertaking.

There are two main pillars of the IMI—safety and efficacy. These are underpinned by two cross-cutting themes: education and training and knowledge management. The SRA is currently focused on five key disease areas: cancer, brain disorders, inflammatory disease, metabolic disease and infectious disease. However, there is a mechanism to allow for evolution of the SRA over the proposed ten years of the programme, so areas can be added or removed as the science develops. It is also intended that the IMI will develop generic technologies that will be widely applicable across many disease areas. The funding will be allocated to IMI projects until 2010, but the funding of projects will continue until 2017. Large amounts of money are being committed by the EU FP7 budget with up to £1 billion from the programme matched by in kind contributions from industry. Thus, the IMI provides real impetus and funding for tackling some of the major bottlenecks in drug discovery.

So how will projects be selected for funding?

The research call topics are proposed by the EFPIA Research Directors Group and then approved by the IMI Board, made up of representatives from industry and the European Commission. The description of the call topics includes an overview of the proposed project with key deliverables and details of the EFPIA participants who have expressed interest in the project. Their role and the in-kind contribution of the industry participants will be described together with expectations from the public consortium that will respond to the call. This private consortium steps back from the process while the public consortia then submit expressions of interest for peer review without the involvement of the private consortium. Public consortia can include representatives from academia and SMA companies as well as patient groups, among others. One of the key features of the IMI and other JTIs is a desire to reduce the bureaucracy usually associated with EU R&D funding programmes. Therefore, this expression of interest essentially comprises brief details of the consortium members and a summary of the scientific rationale in approximately three pages of text. There are some other requirements for information, for example, outline budget plan. These expressions of interest are then subject to an initial peer review resulting in only one successful consortium per call topic that will be invited to write an extensive full proposal. Importantly, this full project proposal will need a draft project agreement as part of the proposal in order to agree the intellectual property rights, among others, up front, before formal approval. All partners are involved in writing this project proposal, including industry, academia, patients, among others. These full proposals are then evaluated by a second peer review committee, which is specific to the therapeutic area and does not include any EFPIA consortia members. This committee will be making evaluations on the basis of the science and on the feasibility of undertaking the project as described.

There are likely to be around 18 topics for the first call that industry has proposed to the Commission for 2008, covering safety prediction, pharmacovigilence, diabetes, brain disorders, respiratory disorders and a number addressing key education and training issues. Topics that are not present in the first round will obviously be important areas for calls in future years. Timings are currently tight for the first call, and the call topics will not be approved until after the first meeting of the IMI Board in early March, before the formal launch of the IMI, which is expected to be in April 2008.

There is, however, enormous enthusiasm and interest across Europe in this initiative, not only from EFPIA companies and academia but also from the SMEs, patient organisations, research charities, other research funders and regulatory bodies. The road ahead will clearly not always be smooth – innovation rarely is – but the IMI represents a real opportunity to make a major difference to biomedical research in Europe. Ultimately this should not only maintain European global research eminence but also make a significant impact on the lives of patients in Europe.

References

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